

## BIRTH DEFECT RISK FACTOR SERIES:

### • SMALL INTESTINAL ATRESIA/STENOSIS

#### ■ DESCRIPTION

Small intestinal atresia is the closure or disconnection of a portion of the small intestine. Small intestinal stenosis involves a narrowing of a portion of the small intestine. Small intestinal atresia/stenosis most frequently affects the duodenum (~50%), followed by the jejunum (~35%), with the ileum (~15%) being least affected (Cragan et al., 1993). Small intestinal atresia/stenosis may affect more than one site of the small intestine (Francannet and Robert, 1996; Cragan et al., 1993). These conditions are usually diagnosed prenatally or shortly after delivery.

Most cases of small intestinal atresia/stenosis do not occur with other birth defects. Duodenal atresia/stenosis is more likely to be associated with other birth defects than are other types of small intestinal atresia/stenosis (Garne et al., 2002; Haeusler et al., 2002; Harris et al., 1995; Cragan et al., 1993; Castilla and Lopez-Camelo, 1990). Approximately 20-30 percent of the cases of duodenal atresia/stenosis are secondary to annular pancreas (Bianchi et al., 2000). Approximately 15-30 percent of the cases of duodenal atresia/stenosis also have chromosomal abnormalities, particularly trisomy 21; chromosomal abnormalities affecting other types of small intestinal atresia/stenosis are less common (Haeusler et al., 2002; Torfs and Christianson, 1998; Kallen et al., 1996; Harris et al., 1995; Cragan et al., 1993).

#### EMBRYOLOGY

At one point in gestation, the duodenum is a solid structure. During the 8th-10th weeks of gestation, a vacuolation process occurs whereby the duodenum becomes a hollow structure. Failure of the vacuolation process may result in duodenal atresia and stenosis (Sencan et al., 2002).

#### ■ DEMOGRAPHIC AND REPRODUCTIVE FACTORS

With respect to **race/ethnicity**, several studies have reported small intestinal atresia/stenosis to be more common in African-Americans than in whites (Harris et al., 1995; Cragan et al., 1993). One investigation observed no significant difference in risk of small intestinal atresia/stenosis in infants born to Vietnamese women compared to infants born to non-Hispanic white women in California (Shaw et al., 2002).

One study failed to identify any **secular trends** in small intestinal atresia/stenosis over time (Cragan et al., 1993). Another found no **seasonal variation** in intestinal atresia rates (Bound et al., 1989).

Review of the literature failed to identify any studies that examined the relationship between small intestinal atresia/stenosis and **geographic location**. One investigation failed to identify any association between duodenal atresia or jejunoileal atresia and **altitude** (Castilla et al., 1999).

The influence of **maternal age** on small intestinal atresia/stenosis risk has been variously reported to be U-shaped (Harris et al., 1995) or higher for women who are less than 20 years of age (Francannet and Robert, 1996), although one study failed to identify any association between maternal age and these defects (Cragan et al., 1993).

No statistically significant relationship between these conditions and **infant sex** has been reported (Haeusler et al., 2002; Harris et al., 1995; Cragan et al., 1993).

Risk for small intestinal atresia/stenosis increases with lower **birth weight** and lower **gestational age** (Rasmussen et al., 2001; Martinez-Frias et al., 2000; Cragan et al., 1993; Mili et al., 1991). Small intestinal atresia has been associated with **intrauterine growth retardation** (Khoury et al., 1988). One investigation reported no effect of **parity** on risk for these defects (Harris et al., 1995). Small intestinal atresia/stenosis is more common among **multiple gestation pregnancies** (Martinez-Frias et al., 2000; Mastroiacovo et al., 1999; Francannet and Robert, 1996; Harris et al., 1995; Cragan et al., 1994; Cragan et al., 1993; Ramos-Arroyo, 1991), although one study reported no association between plurality and small gut atresia (Kallen, 1986).

One study identified higher risk of duodenal atresia with **consanguinity** (Martinez-Frias et al., 2000), while another found no association between parental consanguinity and intestinal atresia (Rittler et al., 2001).

## ■ FACTORS IN LIFESTYLE OR ENVIRONMENT

**Maternal education** does not appear to affect risk for small intestinal atresia/stenosis (Martinez-Frias et al., 2000). One investigation reported no association between **parental farming** occupation and **pesticide** exposure and risk of intestinal atresia (Kristensen et al., 1997). Another investigation failed to identify any significant association between either duodenal atresia or jejunoileal atresia and proximity to various types of **industry** (Castilla et al., 2000). An article that reviewed recent studies of **paternal occupation** and birth defects reported increased risk of small intestinal atresia and paternal occupation of motor vehicle operator (Chia and Shi, 2002).

**Maternal diabetes, hyperthyroidism, hypothyroidism, and other acute and chronic maternal diseases** have not been associated with small intestinal atresia or duodenal atresia, although one study noted increased rates of esophageal/intestinal atresia with preexisting diabetes and gestational diabetes (Aberg et al., 2001). **Maternal infectious diseases** have been suggested to increase risk for ileal atresia (Martinez-Frias et al., 2000; Francannet and Robert, 1996; Becerra et al., 1990; Khoury et al., 1989). One investigation reported no association between maternal **fever, upper respiratory infection, or allergy** and small intestinal atresia/stenosis (Werler et al., 2002).

Prenatal **cocaine** use has been associated with intestinal atresia (Hoyme et al., 1990), although other studies have reported no association between fetal cocaine exposure and birth defects (Behnke et al., 2001). One investigation found elevated rates of small intestinal atresia/stenosis/web with maternal use of **pseudoephedrine** and pseudoephedrine in combination with **acetaminophen** (Werler et al., 2002). **Thalidomide** and **hydantoin** have been linked to increased risk of duodenal atresia (Jones, 1988). One study reported a potential association between **methylene blue** used during amniocentesis and jejunal atresia (van der Pol et al., 1992). **Aspirin, phenylpropanolamine, ibuprofen, antihistamines, guaifenesin, dextromethorphan, vitamins, iron, other minerals, and ovulation induction** have not been reported to increase risk of small intestinal atresia/stenosis (Werler et al., 2002; Martinez-Frias et al., 2000; Francannet and Robert, 1996). Studies have reported no association between **cephalosporin antibiotics, ampicillin, or the benzodiazepines** nitrazepam, medazepam, tofisopam, alprazolam, and clonazepam and intestinal atresia or stenosis (Eros et al., 2002; Czeizel et al., 2001a; Czeizel et al., 2001b).

No association between maternal **folic acid** use and intestinal atresia has been reported (Czeizel et al., 1996). Furthermore, a study that examined **co-trimoxazole**, a combination of trimethoprim and sulfamethoxazole that is a folic acid antagonist, failed to find any association between the medication and atresia/stenosis of the small intestine (Czeizel, 1990).

## ■ PREVALENCE

The reported prevalence for small intestinal atresia/stenosis has shown variation between studies, ranging between 0.6 and 2.3 per 10,000 births for duodenal atresia/stenosis and 0.4 and 1.4 for other small intestinal atresia/stenosis (Table 1). Differences in prevalence may be due to differences in case inclusion criteria.

Table 1. Prevalence per 10,000 births of small intestinal atresia/stenosis					
Reference	Location	Time period	Duodenal atresia/stenosis rate	Other* rate	Total rate
Haeusler et al., 2002	Europe	1996-1998	1.0	1.0	
Martinez-Frias et al., 2000	Spain	1976-1998	0.6	0.4	1.2
Martinez-Frias et al., 2000	Latin America	1967-1996	0.6	0.5	1.2
Torfs and Christianson, 1998	California, USA	1983-1993	2.3		3.9
Stoll et al., 1996	France	1979-1987			3.0
Harris et al., 1995	France	1976-1990	0.7	0.8	
Harris et al., 1995	Sweden	1973-1990	1.1	0.5	

Harris et al., 1995	California, USA	1983-1990	1.0	0.9	
Papp et al., 1995	Hungary	1988-1990	2.0		
Cragan et al., 1993	Georgia, USA	1968-1989	1.4	1.4	2.8
Castilla and Lopez-Camelo, 1990	Central and South America	1982-1986	0.7	0.6	

\*Other small intestinal atresia/stenosis

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*Please Note: The primary purpose of this report is to provide background necessary for conducting cluster investigations. It summarizes literature about risk factors associated with this defect. The strengths and limitations of each reference were not critically examined prior to inclusion in this report. Consumers and professionals using this information are advised to consult the references given for more in-depth information.*

*This report is for information purposes only and is not intended to diagnose, cure, mitigate, treat, or prevent disease or other conditions and is not intended to provide a determination or assessment of the state of health. Individuals affected by this condition should consult their physician and when appropriate, seek genetic counseling.*

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